Original Article

Statistical Mechanics of Neocortical Interactions

Testing Theories with Multiple Imaging Data

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Abstract

To test theories of neocortical processing of macroscopic phenomena, e.g., attention and consciousness, based on relatively microscopic neocortical interactions, e.g., synaptic and neuronal interactions, both theoretical and experimental designs must account for the nonlinear nonequilibrium multivariate stochastic nature of these phenomena. Statistical mechanics of neocortical interactions (SMNI) is one theoretical description that has been tested on short-term memory and electroencephalographic data, and is proposed as a framework to test other theories and mechanisms of neocortical activity. Copula analysis of multivariate stochastic systems, previously developed for financial markets, is an important approach to developing a "portfolio of physiological indicators" to create cost/objective functions to fit experimental data, e.g., multiple synchronous imaging data.

Key Words: statistical physics, nonlinear nonequilibrium, neocortex

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1. Introduction

A theory of columnar neocortical activity has been developed as a statistical mechanics of neocortical interactions (SMNI). This theory has been successful at the columnar scales calculating properties of short-term memory, and has been successful at regional scales calculating circuitries associated with electroencephalography (EEG) measurements.

SMNI, combined with financial risk-management copula analysis has been proposed to enhance resolution of imaging data, when synchronous data among EEG, MEG, PET, SPECT, and/or fMRI, become available. This framework defines multiple sets of data as a portfolio of physiological indicators (PPI).

The above PPI framework of testing theories against experimental data can be applied to other theories than SMNI, especially for other theories that can be developed in a probabilistic setting. Then, this framework also could be used to discriminate these alternative theories based on their goodness of fit to the data with enhanced resolution afforded by PPI.

For example, theories of changes of states of attention, consciousness, etc., associated with large-scale neurophysiology, but dependent on relatively small-scale neuronal interactions, can be explicitly

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included in the SMNI framework, to test the goodness of fit to data, to see if they achieve better explanations of data than other theories.

2. Statistical Mechanics of Neocortical Interactions (SMNI)

As illustrated in Figure 1, SMNI builds from synaptic interactions to minicolumnar, macrocolumnar, and regional interactions in neocortex. Since 1981, a series of SMNI papers has been developed model columns and regions of neocortex, spanning mm to cm of tissue. Most of these papers have dealt explicitly with calculating properties of short-term memory (STM) and scalp EEG in order to test the basic formulation of this approach (Ingber, 1983; Ingber, 1985; Ingber and Nunez, 1995).

Figure 1 illustrates the three biophysical scales of neocortical interactions developed by SMNI (Ingber, 1983). SMNI has developed appropriate conditional probability distributions at each level, aggregating up from the smallest levels of interactions. In (a*) synaptic inter−neuronal interactions, averaged over by mesocolumns, are phenomenologically described by the mean and variance of a distribution Ψ. Similarly, in (a) intraneuronal transmissions are phenomenologically described by the mean and variance of Γ. Mesocolumnar averaged excitatory (E) and inhibitory (I) neuronal firings M are represented in (a'). In (b) the vertical organization of minicolumns is sketched together with their horizontal stratification, yielding a physiological entity, the mesocolumn. In (b') the overlap of interacting mesocolumns at locations r and r' from times t and $t+\tau$ is sketched. In (c) macroscopic regions of neocortex are depicted as arising from many mesocolumnar domains. (c') sketches how regions may be coupled by long−ranged interactions.

2.1. Nonlinear Nonequilibrium Multivariate Statistical Mechanics

Circa 1980, SMNI was the first physical system to use new methods of nonlinear, nonequilibrium, multivariate statistical mechanics to develop multiple scales of synaptic, neuronal, columnar and regional neocortical activity (Ingber, 1981; Ingber, 1982; Ingber, 1983). This algebra was based on calculus originally developed for an approach to quantum gravity (DeWitt, 1957; Cheng, 1972; Graham, 1977; Dekker, 1979; Langouche *et al*, 1982). However, SMNI, e.g., which develops a path-integral approach for neocortical activity, is based on classical physics, albeit specific quantum interactions can be inserted if they can influence the scales of SMNI calculations. Instead of presenting math here, some description and references will suffice to convey the techniques.

2.2. Short-Term Memory (STM)

SMNI studies have detailed that maximal numbers of attractors lie within the physical firing space of excitatory and inhibitory minicolumnar firings, consistent with experimentally observed capacities of auditory and visual STM, when a “centering” mechanism is enforced by shifting background noise in synaptic interactions, consistent with experimental observations under conditions of selective attention (Mountcastle *et al*, 1981; Ingber, 1984; Ingber, 1985; Ingber, 1994; Ingber and Nunez, 1995). This leads to all attractors of the short-time distribution lying along a diagonal line in firing space, effectively defining a narrow parabolic trough containing these most likely firing states. This essentially collapses the 2 dimensional firing space down to a one-dimensional space of most importance. Thus, the predominant physics of STM and of (short-fiber contribution to) EEG phenomena takes place in a narrow “parabolic trough” in firing space, roughly along a diagonal line (Ingber, 1984).

SMNI also calculates how STM patterns may be encoded by dynamic modification of synaptic parameters (within experimentally observed ranges) into long-term memory patterns (LTM) (Ingber, 1983).

SMNI has developed appropriate conditional probability distributions at several levels (Ingber, 1981; Ingber, 1982; Ingber, 1983). Synaptic inter-neuronal interactions are described by the mean and variance of distributions of intraneuronal quanta of chemical transmissions across synaptic gaps. Mesocolumnar averaged excitatory and inhibitory neuronal firings are developed, detailing convergence and divergence of minicolumnar and macrocolumnar interactions. Macroscopic regions of neocortex are developed from many mesocolumnar domains, and SMNI details how regions may be coupled by long-ranged interactions.

SMNI calculates stability and duration of auditory and visual STM (Ingber, 1982; Ingber, 1983; Ingber, 1984; Ingber, 1985; Ingber, 1994; Ingber and Nunez, 1995) as tenths of a second, with capacities of 7±2 (Miller, 1956; Ericsson and Chase, 1982) and 4±2 (Zhang and Simon, 1985) resp., with times of processing information via non-myelinated fibers across minicolumns consistent with time delays associated with internal visual rotations of images. SMNI also explains the primacy versus recency rule of STM (Ingber, 1995), and Hick's law of linearity of reaction time with STM information (Hick, 1952; Jensen, 1987; Ingber, 1999). These time delays are within the same time scales as information processing across regions of cortex via myelinated fibers, thereby permitting synchrony of local and global information within this relatively coarse time resolution.

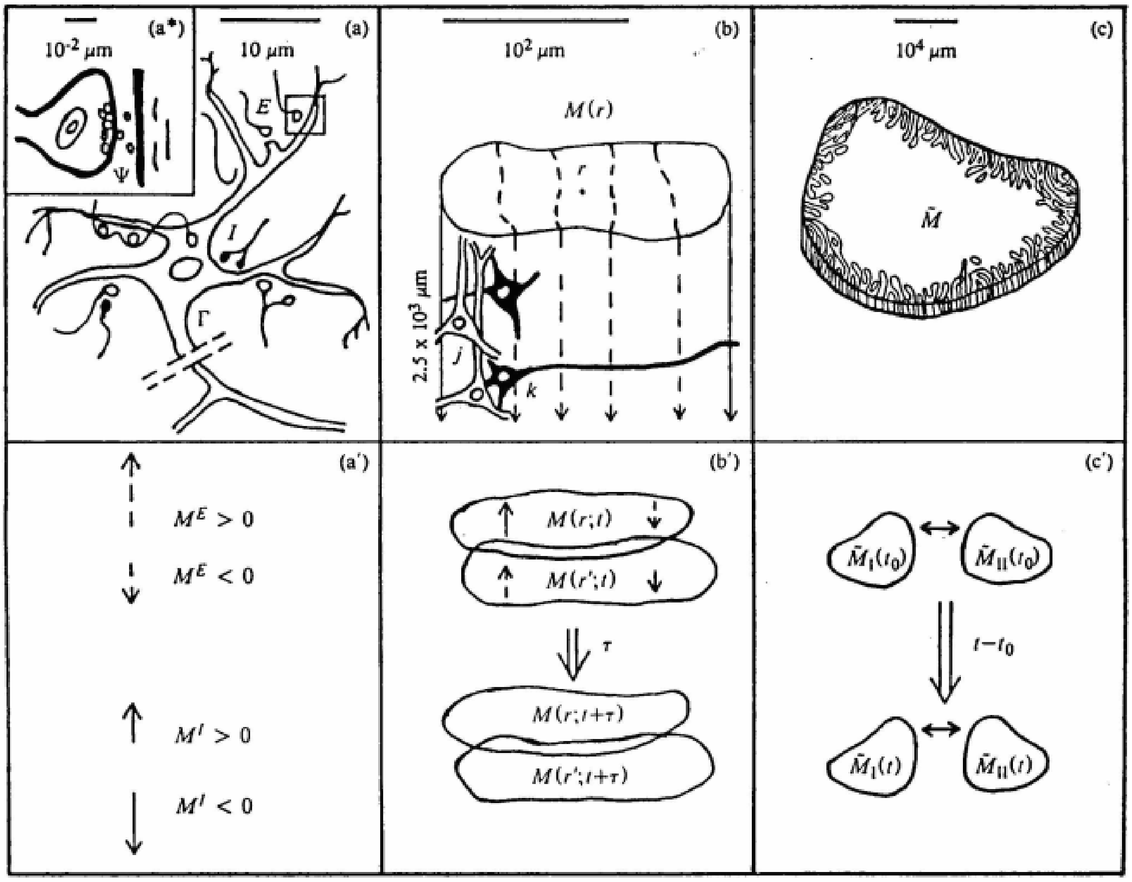

Figure 1. Illustrated are three biophysical scales of neocortical interactions: (a)–(a*)–(a') microscopic neurons; (b)–(b') mesocolumnar domains; (c)–(c') macroscopic regions.

2.2.1. SMNI Description of EEG

Using the power of this formal structure, sets of EEG and evoked potential data from a separate NIH study, collected to investigate genetic predispositions to alcoholism, were fitted to an SMNI model on a lattice of regional electrodes to extract brain "signatures" of STM (Ingber, 1997; Ingber, 1998). Each electrode site was represented by an SMNI distribution of independent stochastic macrocolumnar-scaled excitatory and inhibitory variables, interconnected by long-ranged circuitry with delays appropriate to long-fiber communication in neocortex. The global optimization algorithm Adaptive Simulated Annealing (ASA) was used to perform maximum likelihood fits of Lagrangians defined by path integrals of multivariate conditional probabilities. Canonical momenta indicators (CMI) were thereby derived for individual's EEG data. The CMI give better signal recognition than the raw data, and were used to advantage as correlates of behavioral states. In-sample data was used for training (Ingber, 1997), and out-of-sample data was used for testing (Ingber, 1998) these fits.

A reasonable correlation thereby was made between SMNI and a large set of EEG data, enabling discrimination between subject groups, utilizing specific neuronal circuitry across regions within which processing of events was described by macrocolumar activity. These results gave strong quantitative support for an accurate intuitive picture, portraying neocortical interactions as having common algebraic physics mechanisms that scale across quite disparate spatial scales and functional or behavioral phenomena, i.e., describing interactions among neurons, columns of neurons, and regional masses of neurons.

Since the first SMNI papers, more experience has been gained with larger sets of variables, and it is possible to include laminar circuitry in SMNI. Better correlations can be expected when synchronous multiple imaging is performed (Ingber, 2006b). Similar calculations could be performed within any cortical region, e.g., a sensory or motor region.

3. Additional Physical Interactions

Early SMNI papers noted that background noise of synaptic activity likely would wipe any traces of chaotic or quantum influences. Some detailed calculations on an approach to describe EEG using a chaotic Duffing oscillator, was shown to have no traces at in realistic neocortical activity (Ingber, Srinivasan and Nunez, 1996). No such calculations so far have been performed to test the influence of specific quantum interactions. The columnar scale of SMNI retains an audit trail back to columnar-averaged synaptic activity, and includes interactions and circuitries among short-ranged non-myelinated neuronal fibers and long-ranged myelinated fibers, so it is feasible to insert other specific mechanisms to test against data. The multi-scale SMNI model permits inclusion of explicit time-dependence and nonlinear interactions, without voiding its path-integral properties, which is extremely useful to test in detail intuitions of forces and momenta, CMI, evolving distributions, etc.

In order to apply the SMNI framework to testing theories of neocortical activity, all the computational algebraic modelling above, or some reasonable facsimile, and all the computational algorithms described below, or some reasonable facsimile, must be applied.

4. Computational Algorithms

Some powerful computational algorithms were developed to process this nonlinear stochastic calculus. It is important to stress that the use of these algorithms cannot be approached as a "black-box" statistical analysis of data, e.g., without regard to decisions on scales and tuning of parameters and functions to be developed and tested, and multiple sanity checks on intermediate as well as final results, are typically required.

4.1. Adaptive Simulated Annealing (ASA)

Adaptive Simulated Annealing (ASA) (Ingber, 1993) is used to optimize parameters of systems and also to importance-sample variables. ASA is a C-language code developed to statistically find the best global fit of a nonlinear constrained non-convex cost-function over a D-dimensional space. This algorithm permits an annealing schedule for "temperature" T decreasing exponentially in annealing-time k,

$$T = T_0 \exp(-ck^{1/D}).$$

The introduction of re-annealing also permits adaptation to changing sensitivities in the multi-dimensional parameter-space. This annealing schedule is faster than fast Cauchy annealing, where $T = T_0/k$, and much faster than Boltzmann annealing, where $T = T_0/\ln k$. ASA has over 100 OPTIONS to provide robust tuning over many classes of nonlinear stochastic systems.

For example, ASA has ASA_PARALLEL

OPTIONS, hooks to use ASA on parallel processors, which were first developed in 1994 when the author of this approach was PI of National Science Foundation grant, Parallelizing ASA and PATHINT Project (PAPP). For a score of years, these OPTIONS have been used by many researchers and companies, providing valuable feedback to the open-source ASA code.

4.2. PATHINT and PATHTREE

In some cases, it is desirable to develop a time evolution of a short-time conditional probability, e.g., of the kind fitted in this study to EEG data. Two useful algorithms have been developed and published by the author. PATHINT and PATHTREE have demonstrated their utility in statistical mechanical studies in finance, neuroscience, combat analyses, neuroscience, and other selected nonlinear multivariate systems (Ingber, Fujio and Wehner, 1991; Ingber and Nunez, 1995; Ingber, 2000). PATHTREE has been used extensively to price financial options (Ingber, Chen *et al*, 2001).

4.3. Trading in Risk Dimensions (TRD)

There are often two kinds of errors committed in multivariate analyses: E1: Although the distributions of variables being considered are not Gaussian (or not tested to see how close they are to Gaussian), standard statistical calculations appropriate only to Gaussian distributions are employed. E2: Either correlations among the variables are ignored, or the mistakes committed in (E1) — incorrectly assuming variables are Gaussian — are compounded by calculating correlations as if all variables were Gaussian.

The harm in committing errors E1 and E2 can be fatal — fatal to the analysis and/or fatal to people acting in good faith on the basis of these risk assessments. Risk is measured by tails of distributions. So, if the tails of some variables are much fatter or thinner than Gaussian, the risk in committing E1 can be quite terrible. Many times systems are pushed to and past desired levels of risk when several variables become highly correlated, leading to extreme dependence of the full system on the sensitivity of these variables. It is very important not to commit E2 errors.

A full real-time risk-managed trading system has been coded by the author using state of the art risk management algorithms, Trading in Risk Dimensions (TRD) (Ingber, 2005). TRD is based largely on previous work in several disciplines using a similar formulation of multivariate nonlinear nonequilibrium systems (Ingber, 2001c; Ingber, 2001d; Ingber, 2001b), using powerful numerical algorithms to fit models to data (Ingber, 2001a). A report which was a precursor to this project was formulated for a portfolio of options (Ingber, 2002).

In the context of this approach, the concepts of “portfolio” are considered to be extended to the total ensemble of of multiple regions of populations of data, each having sets of multiple variables. That is, although each region may have the same kinds of multiple variables, to create a generic system for the project, such variables in different regions are part of the full set of multivariate nonlinear stochastic variables across all regions. Once the full “portfolio” distribution is developed, various measures of cost or performance can be calculated, in addition to calculating various measure of risk/uncertainty of performance.

The concepts of trading-rule parameters can be extended to how to treat parameters that might be included in this work, e.g., to permit some top-level control of weights given to different members of ensembles, or parameters in models that affect their interactions, towards a desired outcome of projects.

4.3.1. Gaussian Copula

Gaussian copulas are developed in TRD (Ingber, 2005). Other copula distributions are possible, e.g., Student-t distributions (often touted as being more sensitive to fat-tailed distributions — here data is first adaptively fit to fat-tailed distributions prior to copula transformations). These alternative distributions can be quite slow because inverse transformations typically are not as quick as for the present distribution. The copula-transformed multivariate distribution can be used to develop a cost function to fit theoretical models to experimental data, thereby establishing a framework for developing measures of performance of competing theoretical models of specific neocortical phenomena.

Copulas are cited as an important component of risk management not yet widely used by risk management practitioners (Blanco, 2005). Gaussian copulas are presently regarded as the Basel II standard for credit risk management (Horsewood, 2005). TRD permits fast as well as robust copula risk management in real time.

The copula approach can be extended to more general distributions than those considered here (Ibragimon, 2005). If there are not analytic or relatively standard math functions for the transformations (and/or inverse transformations described) here, then these transformations must be performed explicitly numerically in code such as TRD.

4.3.2. Scales of Interaction

Figure 2 illustrates the flow of algebra across multiple scales using the above computational techniques.

“Learning” takes place by presenting the MNN with data, and parametrizing the data in terms of the firings, or multivariate firings. The “weights,” or coefficients of functions of firings appearing in the drifts and diffusions, are fit to incoming data, considering the joint “effective” Lagrangian (including the logarithm of the prefactor in the probability distribution) as a dynamic cost function. This program of fitting coefficients in Lagrangian uses methods of ASA.

“Prediction” takes advantage of a mathematically equivalent representation of the Lagrangian path−integral algorithm, i.e., a set of coupled Langevin rate−equations. A coarse deterministic estimate to “predict” the evolution can be applied using the most probable path, but PATHINT has been used. PATHINT, even when parallelized, typically can be too slow for “predicting” evolution of these systems. However, PATHTREE is much faster.

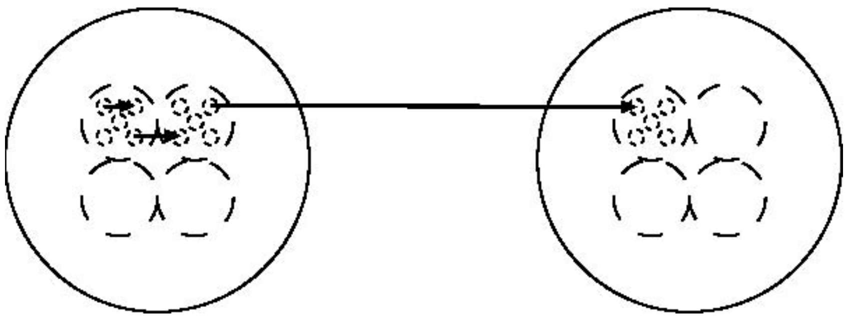

Figure 2. Scales of interactions among minicolumns are represented, within macrocolumns, across macrocolumns, and across regions of macrocolumns.

4.4. Portfolio of Physiological Indicators (PPI)

It is clear that the SMNI distributions also can be used to process different imaging data beyond EEG, e.g., also MEG, PET, SPECT, fMRI, etc., where each set of imaging data is used to fit its own set of parameterized SMNI distributions using a common regional circuitry. Different imaging techniques may have different sensitivities to different synaptic and neuronal activities. For example, neural circuits perpendicular to the scalp give rise to most measurable EEG; neural circuits parallel to the scalp give rise to most measurable MEG. Then, portfolios of these imaging distributions can be developed to describe the total neuronal system, a portfolio of physiological indicators (PPI), e.g., akin to a portfolio of a basket of markets. For example, this could permit the uncertainties of measurements to be reduced by weighting the contributions of different data sets, etc. Overlaps of distributions corresponding to different subsets of data give numerical specificity to the values of these subsets.

It is to be expected that better resolution of behavioral events can be determined by joint distributions of different imaging data, rather than by treating each distribution separately. The PPI project awaits such multivariate synchronous data.

The TRD project illustrates how multiple non-Gaussian distributions can be developed for use as cost functions to fit data (Ingber, 2005). The generic concept of a portfolio has been extended to PPI (Ingber, 2006b), as well as to artificial intelligence, developing ideas by statistical mechanics (ISM) to calculate risk and uncertainty of generic “ideas” that arise in many systems (Ingber, 2006a; Ingber, 2007; Ingber, 2008). These generic applications demonstrate that many classes of phenomena may be included in this framework.

5. Conclusion

A framework is developed to test theories of neocortical processing of macroscopic phenomena based on relatively microscopic neocortical interactions. Both theoretical and experimental designs must account for the nonlinear nonequilibrium multivariate stochastic nature of these phenomena. Statistical mechanics of neocortical interactions (SMNI) has been developed as such a framework, which has been tested on short-term memory and electroencephalographic data, and is proposed as a framework to test other theories and mechanisms of neocortical activity.

Several computational algorithms must be used for such models, including methods of global optimization and sampling, and time evolution of probability distributions. Copula analysis of multivariate stochastic systems, previously developed for financial markets, is another important computational tool used to develop cost/objective functions suitable for fitting and testing theoretical models against experimental data.

The inherent nonlinearity of these theoretical and experimental aspects of neocortical processing make it unlikely that this approach to test theories might introduce any “circular” logic of confounding fitted resolutions of theoretical and experimental paradigms. For example, a maximum likelihood optimization of fitting probability models to imaging data is used to find measures of fit to data, which can help discern among competing theories.

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